

REMARKS/ARGUMENTS

Amendments to the claims.

Claims 1-70 were previously canceled. Claims 73 and 79-82 are instantly canceled.

Claims 71-72 are instantly amended. Claims 83-89 are newly added.

After entry of this amendment, claims 71-72, 74-78, and 83-89 will remain in this application.

Support for “95%” and 98% identity to SEQ ID NO: 4 may be found, for example, on page 54, lines 2-4, lines 6-7, and lines 20-23.

Support for a method of producing and selecting a plant exhibiting greater tolerance to water deprivation may be found on, for example, page 83, lines 3-8 (including: “After transformed plants are selected and grown to maturity, those plants showing a modified trait are identified. The modified trait can be any of those traits described above”; water deprivation is described above this line on, for example, page 3, line 1, on page 5, lines 15-20, and on page 21, line 14), on page 151, lines 32-35, on page 119, lines 2-3, and in claim 25(e).

No new matter is added by this amendment. This amendment is being made in response to the pending Office action and was not made previously for that reason. Entry of this amendment is respectfully requested.

Response to specific items of the Office action.

Items 6, and 7. Rejection under 35 U.S.C. §112, first paragraph.

Claims 71-73 and 75-79 have been rejected under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement. Applicants believe this rejection has been avoided by the present amendment of the claims.

The claimed genus is to G922, SEQ ID NO: 4 and sequences that are closely related to G922. The pending claims recite a functional limitation, i.e., conferring greater tolerance to water deprivation as compared to a control plant, and also require a predictable structure of at least 95% amino acid sequence identity to SEQ ID NO: 4,

Applicants have provided in Table 1 the identifying structural elements: the three

conserved SCR domains that are homologous to that of SEQ ID NO: 4 through sequence alignments as shown in Figure 19A-19R, and also described a fourth “scr/pro-rich domain that is unique to the G922 clade (lines 11-12 at page 10). Applicants have also disclosed the conserved structural elements, i.e., the three conserved SCR domains corresponding to amino acids 134-199, 332-401 and 405-478 of SEQ ID NO: 4, which are present in closely sequences that have functioned by conferring water deprivation tolerance. Since these sequences are derived from diverse plant species, (both *Arabidopsis* and soy), they represent a practical sampling of a large number of sequence species. Applicants believe that in view of the significant structure/function relationships disclosed in the cited references and conserved domain disclosed in the specification in combination with the disclosed working examples, one of ordinary skill in the art would recognized that sequences and three conserved domains with a high degree of identity to SEQ ID NO: 4 correlate with the function of conferring greater tolerance to water deprivation.

Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph, for lack of written description, be withdrawn.

Items 8 and 9. Rejection under 35 §U.S.C. 103 (a).

The Office action rejected the previously pending claims 71-79 under 35 U.S.C. §103(a) based on Benfey et al (WO97/41152) in view of Benfey et al (U.S. Patent 6,411,270, filed 24 April 1997) and Pysh et al (1999, *Plant Journal* 18 (1): 111-119).

As indicated in the last response, the inventor of U.S. Patent 6,411,270 is Toshifumi Ohsawa, not Benfey, nor does the referred patent concerns DNA or protein sequences. It is believed the Examiner is referring to 6,441,270.

The method claims.

Applicants believe the newly introduced method claims are not made obvious by any combination of the cited references. These references do not suggest the production and selection of transformed plants that are more tolerant to water deprivation than a control plant. At best, the 6,441,270 patent describes the “screening for the marker gene traits” or “identif[ication of] a plant or plant cell transformant containing the gene constructs”.

The composition claims.

This rejection of transgenic plant claims is respectfully traversed for the reason set forth below.

The amended claims are directed to plants that overexpress the claimed sequences

As the Examiner has indicated, “the instant claims are not limited to overexpression” (instant Office action, page 11).

In response, Applicants note that the claims are now “limited to overexpression”.

The Pysh sequence is incomplete.

Applicants again note that Pysh did not disclose the complete sequence of SCL3 (syn. SRPa3). A band in a DNA gel can hardly be regarded as representing any specific structure of a full length DNA molecule. Pysh did not teach the presently claimed sequences. The only related sequence in Pysh’s disclosure lacks the *157 amino acids* of the instant SEQ ID NO: 4, *including the 24 amino acids that make up the first conserved SCR domain*. Combining Pysh and Benfey does not cure the deficiency of lacking the structure of the full length sequence, and the combination of Benfey and Pysh fails to cure the deficiency of lacking the functional limitation of conferring greater tolerance to water deprivation since there is no known evidence that the Pysh sequence would function in any regard let alone with the claimed function.

The Benfey sequence is not close enough to the instantly claimed sequences to make the claimed plants obvious, and the possible options between Benfey and Pysh were not known or finite.

As previously indicated, the Examiner has acknowledged that the Benfey sequence is not being claimed. To underscore the phylogenetic differences between SCR and SCL3, Pysh states that “Three members, SCR, SCL3 and SCL8, do not group with any of the other sequences (page 115, col. 1)” and “Most importantly, SCL3 does not have significant stretches of absolute sequence homology at the nucleotide level with SCR or with any other member of the family” (page 116, col. 2).

If the possible options were not either known or finite, then an obvious to try rationale cannot be used to support a conclusion of obviousness (*Rolls-Royce, PLC v. United Technologies Corp.*, 603 F.3d 1325 (Fed. Cir. 2010)). The SCR protein sequence disclosed by Benfey is not sufficiently related to the instantly claimed SEQ ID NO: 4 to make obvious any attempt to produce transgenic plants with the latter. In a BLASTp analysis comparing the 653

amino acids of SCR to SEQ ID NO: 4, even the most similar regions contain 89 of 248 identical residues. That is, there is only about 35% identity over the most similar 42% of the SCR protein sequence:

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SCR: 241 ERENSSTDAPPOFETVTVATVAVQNTAALERKEEIKROKQDEEGLHLTLLOQAEA 300
      N P V T T A A K K E G L L L L C A
G922: 6 QEDNGTSSVASSPQVFTSM-SLNRPTLLASSPPHCLKDLKPEERGLYLIHLLLTCA 64
      N P V T T A A K K E G L L L L C A
SCR: 301 VSADNLEEANKLLLEISQLSTPYGTSAQRVAAYFSEAMSARLLNSCLGIYAALPSRWMPQ 360
      V L A N L S L P G Q R A A Y F E A R L S G Y A L
G922: 65 VASGLQNAANAALQLSHLASPDGTMQRIAAAYFTEALANRLKSWPGLYKALNATQTRT 124
      V L A N L S L P G Q R A A Y F E A R L S G Y A L
SCR: 361 THSLKMQVASQFVNGISPLVKFSHTANQAIQAEFEKEDSVHIIIDLDIMOGLOWPGLFHI 420
      F P K S N A I E A E E V H I D L Q W L
G922: 125 NNVSEEIHVRRLFEMFFILKVSYLLTNRAILEAEKEGKVMHVHIDLDAPEAPWALLQA 184
      F P K S N A I E A E E V H I D L Q W L
SCR: 421 LASRPGPPPHVRLTGLGTSMEALQATGKRLSDFTDKLGLPFPEFCPLAEKVGNLDERLNV 480
      SRP GPPH R T G H E L R L K L P F F P L E L V
G922: 185 FNSRPEGPHLIRTVGHQKEVLEQMAHRLIEEAKEKLDIPFQFNPVVSRDLCLNVEQLRV 244
      SRP GPPH R T G H E L R L K L P F F P L E L V
SCR: 481 RKREAVAV 488
      EA AV
G922: 245 KTGEALV 252
      EA AV

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Since the Office has affirmed that “tolerance to the recited water deprivation types ... is controlled by many different physiological pathways” (Office action of September 10, 2008), and given that G922 is only about 35% identical over the most similar 42% of the SCR protein sequence, it seems reasonable to expect that the Office would not grant claims that reach to the G922 sequence based on a disclosure of the SCR protein sequence, since there would be little reasonable expectation of success given “the quantity of experimentation that would be necessary” (for 60% and greater identity, Office action of September 10, 2008). Where there was reason to select and modify the lead compound to obtain the claimed compound, but no reasonable expectation of success, the claimed compound would not have been obvious (Federal Register, Vol. 75, No. 169, September 1, 2010).

The above differences, the partial sequence taught by Pysh, and the lack of any teaching of the instant traits by the combined art references underscore the fact that no expectation of success of producing G922-overexpressing transgenic plants that have greater tolerance to water deficit can be found by the Office without Applicants' own disclosure in hand. The Supreme Court has "warn [ed] against 'temptation to read into the prior art the teachings of the invention in issue' and instruct[ed] courts to 'guard against slipping into the use of hindsight.'" *KSR Int'l v.*

Teleflex Inc., 127 S. Ct 1742 (2007), quoting *Graham v. John Deere Co.*, 383 U.S. at 36.

Therefore, the claimed plants are not obvious over the combination of Benfey and Pysh.

Thus, the Benfey sequence is not particularly similar to the claimed sequence, there is a sizable gap between SCR and SEQ ID NO: 4, and so the possible options between SCR and SEQ ID NO: 4 were not known or finite. Furthermore, water deprivation tolerance is only one of the very large number of possible phenotypes that a plant could have and that were not suggested or tested by Benfey.

The art combination does not expressly or inherently predict plants with the instant traits.

The combination of the Benfey and Pysh disclosures does not make obvious transformed plants with greater water deficit for a number of reasons, including the fact that the combination of the prior art does not predict the instant plants with the instant traits, expressly or inherently. The Office, by alleging that greater tolerance to water deficit is an inherent but unknown function of the transgenic plants expressing G922 based on Benfey's disclosure, and that "one of ordinary skill in the instant art would have made a large number of transgenic plants and hence would have made the claimed transgenic plant" (Office action, page 9), does not sufficiently consider the Federal Circuit's reasoning when it decided that inherency cannot be "established by probabilities or possibilities" and that, the mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Robertson*, 49 USPQ2d 1949, 1951 (Fed. Cir. 1999). The court stated that the burden falls on the examiner to "provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original). The Office action has not provided a factual basis or technical reasoning to support a finding of inherency based on Benfey or Pysh. Applicants' own experimental evidence demonstrated that greater tolerance to water deficit does not necessarily flow from overexpression of the claimed sequences. As shown in the previously submitted declaration of Dr. Reuber, not all transgenic plants overexpressing G922 displayed greater tolerance to water deficit: four lines did, but sixteen lines showed no discernible difference compared to control plants. Thus, the claimed traits are not necessarily present in the hypothetical combination.

Regarding what constitutes inherency, please see *Toro Co. v. Deere & Co.*, 355 F.3d

1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004)("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention.") (*emphasis added*).

"The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter *is necessarily present in the thing described in the reference*, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. *The mere fact that a certain thing may result* from a given set of circumstances *is not sufficient.*' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted). (MPEP 2112(IV) (*emphasis added*).

Therefore, water deficit tolerance is not necessarily present, and thus not an inherent trait or function of transgenic plants expressing SRPa3.

Applicants respectfully submit that it is not the transgenic plants transformed with the full length sequence of G922 that were claimed by the instant application, but rather a specific subset of those that have water deficit tolerance. Even if the complete sequence of G922 were obtainable before Applicants' disclosure, no trait of water deficit tolerance has ever been suggested for transgenic plants transformed with G922 polynucleotide by Benfey or Pysh. Please see MPEP 2144.08 (II): "The fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness. *In re Baird*, 16 F. 3d 380, 382, 29 USPQ2d 1550, 1552 (Fed Cir. 1994) ("the fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious." MPEP 2144.08 requires "Office personnel should ascertain the difference between the closest disclosed prior art species or subgenus of record and the claimed species or subgenus, ... and compare it to the claimed species or subgenus to determine the differences, ... make explicit findings on the similarities and differences between the closest disclosed prior art species or

subgenus of record and the claimed species or subgenus including findings relating to similarity of structure, chemical properties and utilities.” As we have seen with the evidence presented in Dr. Reuber’s declaration submitted previously to the Office, the instantly claimed genus, i.e., plants overexpressing G922 (SEQ ID NO: 4) and having greater water deficit tolerance, do not have thicker root development; quite on the contrary, a number of the overexpressors had less root development than control plants. Thus, the claimed trait associated with the claimed sequences must be viewed as surprising and inventive.

Furthermore, from a practical standpoint, there is no reason to believe that “one of ordinary skill in the instant art would have made a large number of transgenic plants and hence would have made the claimed transgenic plant”. In fact, if one of ordinary skill is going to test a large number of transcription factor sequences, there is a practical upper limit to the number of plants one can reasonably make and test, and that’s just for overexpressors (twice as many plants would be involved if one also wanted to test knock-outs, with the number increased further for knock-downs). So, no, one of ordinary skill in the instant art would not have made a large number of transgenic plants overexpressing SCL3 unless one had some motivation to focus on SCL3 rather than other promising transcription factors. And given a lack of a water deprivation tolerance teaching in the art and the discovery of some plant lines with smaller roots than controls, the motivation to produce a large number of plants could very well be lacking.

The claimed plants involve additional complexity as compared with the prior art

To start with the Benfey disclosure and reach plants transformed with the sequence of Pysh, one would have to predict that a large number of sequences related to SCR would function similarly, determine the full-length sequence based on Pysh’s partial sequence, clone and transform the sequences into plants, and test for the instantly claimed trait that was not suggested by the art references.

Predictability as discussed in KSR encompasses the expectation that prior art elements are capable of being combined, as well as the expectation that the combination would have worked for its intended purpose. However, the prior art does not provide the instantly claimed known function, and thus the instant disclosure yields more than predictable results. Transgenic plants claimed in the instant application not only comprise sequences with predictable, disclosed structural elements (for example, three conserved domains) and an overall protein structure by

95% percent identity, but also have greater tolerance to water deprivation compared to control plants. The MPEP requires that “Examiners must account for all claim limitations in their rejections by explaining how each limitation is disclosed or rendered obvious by the reference(s) applied. ‘All words in a claim must be considered in judging the patentability of that claim against the prior art’” *In re Wilson*, 424 F. 2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970) MPEP 2143.03. The Office action did not take into account the functional limitation that is crucial for identifying the claimed genus. Benfey’s prediction that SCR proteins have the abilities to confer thicker root does not make plants that over-express SCR proteins and have greater tolerance to water deficit obvious. 35 U.S.C. 103(a) demands consideration of “the subject matter sought to be patented.. as a whole” (MPEP 2141). When asserting a *prima facie* case of obviousness, “the burden falls on the Examiner to show.. that a person of ordinary skill in the art would have had reason to attempt to ... carry out the claimed process, and would have had a reasonable expectation of success in doing so.” *Pharmastem Therapeutics v. Viacell, Inc.* 491 F.3d 1342, 1360 (Fed cir. 2007). The reasoning provided by the Office does not explain why water deprivation tolerance is predictable (or inherent) in view of the plants transformed with the partial sequence or the full length counterpart and having thicker root development.

If results would not have been predictable, Office personnel should not enter an obviousness rejection using the combination of prior art elements rationale, and should withdraw such a rejection if it has been made.

Accordingly, Applicants respectfully request the rejection under 35 U.S.C. §103(a) be withdrawn.

CONCLUSION

Applicants believe that no additional fee is due with this communication. However, if the USPTO determines that an additional fee is due, the Commissioner is hereby authorized to charge Mendel Biotechnology, Inc. Deposit Account No. 50-1025.

Respectfully submitted,
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